REMARKS

Claims 1-48 are pending in the subject application. By this Amendment, applicants have canceled claims 1-16 and 41, added new claim 49, and amended claims 17-20, 36 and 39. Claims 25-35, 37-38, 40 and 42-48 are withdrawn from consideration by the Examiner. Accordingly, claims 17-40, and 42-49 are pending in the subject application.

Exhibit A annexed hereto sets forth the amended paragraph on page 1, lines 1-4, which has been marked up to show the changes relative to the previous version thereof.

The changes to claims 17-20, 36 and 39 are set forth in the claims attached as **Exhibit B** which have been marked up to show the changes relative to those previously pending claims.

Support for the amendments to the claims and the addition of new claim 49 can be found throughout the specification, including, inter alia, as follows:

claim 17, page 16, lines 5-10;
claim 18, page 17, lines 1-3, 16-18;
claim 19, page 17, lines 26-28;
claim 20, page 17, lines 30-31, to page 18, line 1;
claim 36, page 4, lines 16-27, page 7, lines 27-31, to page 8, lines 1-2, page 16, lines 5-10, page 28, lines 27-31, page 29, lines 1-3;
claim 39, page 4, lines 16-27, page 29, lines 19-31, and
claim 49, page 4, lines 16-27, page 16, lines 5-10, page 17, lines 16-24, page 28, lines 9-14, page 33, lines 9-14.

Applicants submit that these amendments are fully supported by the specification and do not raise any issue of new matter.

Therefore, applicants respectfully request that these amendments be entered. Upon entry of the Amendment, claims 17-24, 36, 39 and 49 will be under examination.

Rejoinder of Claims

The Examiner stated that applicants' argument as to rejoinder of claims in Groups I and II is agreed with and therefore Groups I and II, namely claims 1-24, 36, 39 and 41, will be examined together.

Claim of Priority

The Examiner stated that in their amendment to the first paragraph of the specification, applicants make reference to PCT/EP97/05198 as the 35 U.S.C. §371 priority application for this application, but do not make reference to 08/718,661, which is also claimed in the oath as having 35 U.S.C. §120 priority. The Examiner stated that a statement to this effect must be included in the first paragraph along with an indication whether this is a continuation, continuation-in-part or divisional application.

In response, applicants have amended the first paragraph of the specification to state that this application claims priority of, and is a continuation-in-part of U.S. Serial No. 08/718,661, now U.S. Patent No. 5,876,972.

Information Disclosure Statement

The Examiner stated that the Information Disclosure Statement (IDS) filed March 15, 1999 had a PTO-1449 form attached. However, the Examiner stated that approximately as many documents listed on the PTO-1449 form were also apparently submitted with no PTO-1449 form. The Examiner stated that if applicants wish to have these documents considered they should submit a PTO-1449

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form listing them.

In response, the Examiner was contacted by telephone on August 30, 2001 by Chris M. Ries, Esq. of the office of the undersigned attorney to confirm that no additional references were before the Examiner that were not listed on the PTO-1449 form filed with applicants' IDS on March 15, 1999. The Examiner noted that the error was due to the presence of duplicate copies of the listed references, and indicated that therefore, no further action in this regard need be taken by applicants.

Rejection under Non-statutory Double Patenting

The Examiner rejected claims 1-16 and 19-24 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-24 of U.S. Patent No. 5,876,972 (the '972 patent).

The Examiner alleged that although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims claim essentially the same thing as the claims of the '972 patent, with only minor differences in wording.

In response to the rejection of claims 1-16, without conceding the correctness of the Examiner's position and solely to advance prosecution, applicants have canceled claims 1-16, thereby rendering the rejection thereof moot.

In response the rejection of claims 19-24, applicants respectfully traverse. Applicants submit that these claims are patentably distinct from the claims of the '972 patent. Specifically, claim 17 provides a nucleic acid molecule comprising (a) a nucleotide sequence encoding the amino acid

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sequence given in SEQ ID NO.: 17 or (b) the nucleotide sequence given in SEQ ID NO.: 16. Nowhere are SEQ ID NOS.: 16 or 17 taught or suggested in any of claims 1-24 of the '972 patent. Moreover, these sequences correspond to the human ZAC gene which encodes a tumor suppressor protein. Applicants maintain that one of ordinary skill in the art would not have been able to predict these human ZAC gene-related sequences, absent experimentation, in view of claims 1-24 of the '972 patent. For these reasons, claims 19-24, which depend from claim 17, are not obvious over the claims of the '972 patent. Consequently, applicants respectfully request that this ground of rejection be withdrawn.

Rejection under 35 U.S.C. §101

Claim 12 is rejected under 35 U.S.C. §101 because the claimed invention allegedly lacks patentable utility.

In response, without conceding correctness of the Examiner's position and solely to advance prosecution, applicants have canceled claim 12, thereby rendering the rejection moot.

Claim 41 is rejected under 35 U.S.C. §101 because it is drawn to allegedly non-statutory subject matter.

The Examiner stated that use claims are not allowed in U.S. patent practice, therefore, the claim should be drawn to a method with distinct steps.

In response, but without conceding the correctness of the Examiner's rejection, applicants have canceled claim 41 and replaced it with new claim 49. New claim 49 provides "a method for treating, preventing, or delaying the reoccurrence of a disorder in a subject related to or dependent on the modulation of a protein comprising the amino acid sequence of SEQ ID NO.:

2 or SEQ ID NO.: 17, comprising administering to the subject an effective amount of a nucleic acid molecule of at least 15 nucleotides in length which, under stringent hybridizing conditions, hybridizes specifically to a nucleic acid molecule (i) coding for the amino acid sequence of SEQ ID NO.: 2, (ii) comprising the nucleotide sequence of SEQ ID NO.: 1,(iii) coding for the amino acid sequence of SEQ ID NO.: 17, (iv) comprising the nucleotide sequence of SEQ ID NO.: 16, or (v) having a sequence complementary to the nucleic acid molecule as defined in (i),(ii),(iii), or (iv)."

Applicants maintain that new claim 49 satisfies the requirements of 35 U.S.C. §101.

Rejection under 35 U.S.C. §112, Second Paragraph

Claims 1-2, 4, 7, 12, 36 and 41 are rejected under U.S.C. 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Examiner alleged that claim 1 is indefinite in the recitation of "nucleic acid molecules hybridizing to a nucleic acid molecule as defined in (a) or (b)", and that there is no indication of stringency or size. The Examiner stated that almost any nucleic acid will hybridize to another if the stringency is low enough and/or if it is small enough.

The Examiner further alleged that claim 2 is indefinite in the recitation of "optionally" on line 17 and is also indefinite in the recitation of "pool(s)" twice and "vector(s)" once. The Examiner stated that it is not clear whether the singular or plural is desired.

The Examiner also alleged that claim 4 is indefinite in the recitation of "the peptide PACAP". The Examiner stated that to the ordinary artisan reading this claim "PACAP" would indicate "Pro-Ala-Cys-Ala-Pro", and apparently "pituitary adenylate cyclase activating peptide" was intended.

In addition, the Examiner alleged that claim 7 is indefinite in the recitation of "MMTV", and apparently "mammary mouse tumor virus" was intended.

Further, the Examiner alleged that claim 12 is indefinite in the recitation of "hybridizes to a nucleic acid molecule of claim 1". The Examiner asserted that if a molecule is short enough and/or if the hybridization conditions have a low enough stringency, almost any molecule will hybridize with another. The Examiner also alleged that it is also confusing and indefinite in the recitation of "said mutated version" on line 2 and that the term does not have antecedent basis in claim 1.

The Examiner also alleged that claim 20 is indefinite in the recitation of "and/or" and stated that it is not clear whether the vector must be expressed in both prokaryotic and eukaryotic cells or only one.

Finally, the Examiner alleged that claim 41 is indefinite in the recitation of "and/or" on line 3. The Examiner asserted that it is not clear from the instant recitation whether the cumulative or alternative is desired.

In response to rejection of claims 1, 2, 4, 7, 12, 20 and 41, without conceding the correctness of the Examiner's position and solely to advance prosecution, applicants have canceled these claims, thereby rendering the rejection thereof moot.

Applicants point out that new claim 49, corresponding to canceled claim 41, does not recite any of the language objected to by the Examiner.

The Examiner alleged that claim 36 is indefinite in the recitation of "hybridizing conditions" on line 5 and "hybridized" on line 6. The Examiner stated that almost any nucleic acid will hybridize to another if it is short enough or the stringency of the hybridization is low enough.

In response, without conceding the correctness of the Examiner's position and solely to advance prosecution, applicants have amended claim 36 to recite the term "stringent" hybridizing conditions and state that the mRNA is "specifically" hybridized to the probe. Page 7, lines 27-31, to page 8, lines 1-2, of the specification define stringent conditions for hybridization. Therefore, applicants submit that a person skilled in the art would know how to practice the method of claim 36. Accordingly, applicants respectfully request that this ground of the rejection be withdrawn.

Rejection under 35 U.S.C. §112, First Paragraph

Claim 41 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was allegedly not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner stated that claim 41 is drawn to using the 15 nucleotide long nucleic acid molecule of claim 18 to treat, prevent or delay reoccurrence of a disease in a subject. The Examiner asserted that the specification does not teach that this 15 nucleotide long nucleic acid molecule has ever been used to

treat, prevent or delay reoccurrence of a disease in a subject and therefore there is nothing that would make one of ordinary skill in the art believe this would work.

In response, applicants respectfully traverse this rejection. Applicants again point out that claim 41 has been canceled and replaced with new claim 49 in order to comply with certain format requirements. Applicants understand the Examiner's rejection to apply to new claim 49.

Again, claim 49 provides a method for treating, preventing, or delaying the reoccurrence of a disorder in a subject which disorder is related to or dependent on the modulation of a protein comprising the amino acid sequence of SEQ ID NO.: 2 or SEQ ID NO.: 17, comprising administering to the subject an effective amount of a nucleic acid molecule of at least 15 nucleotides in length which, under stringent hybridizing conditions, hybridizes specifically to a nucleic acid molecule (i) coding for a polypeptide comprising the amino acid sequence of SEQ ID NO.: 2, (ii) comprising the nucleotide sequence of SEQ ID NO.: 1,(iii) coding for the amino acid sequence given in SEQ ID NO.: 17, (iv) comprising the nucleotide sequence given in SEQ ID NO.: 16, or (v) being a sequence complementary to the nucleic acid molecule as defined in (i),(ii),(iii), or (iv).

The Examiner is reminded that enablement under §112, first paragraph may be satisfied using information found in the art. That is if one skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation, then the invention is enabled. See M.P.E.P. 2164.01(a).

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Sheet 1 of 1

Form PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 52130-A-PCT-US	Serial No. 09/254,870
INFORMATION DISCLOSURE CITATION (Use several sheets if necessary)		Applicants Dietmar Spengler and Laurent Journot	
		Filing Date August 16, 1999	Group 1652

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

CM	AJ	Pagotto, et al., (1999) "Inhibition of Zac1, a New Gene Differentially Expressed in the Anterior Pituitary, Increases Cell Proliferation" , Endocrinology, 140, No.2, 987-996 ~~(Exhibit 1); and~~
CM	AJ	Gillardon, et al., (1998) "Delayed Up-regulation of Zac1 and PACAP Type I Receptor after Transient Focal Cerebral Ischemia in Mice", Molecular Brain Research, 61, 207-210 ~~(Exhibit 2)~~

EXAMINER	DATE CONSIDERED
[signature]	9/27/01

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Contrary to the Examiner's position, applicants maintain that one skilled in the art would know how to practice the claimed method based on the specification and the art at the time of filing. More specifically, applicants maintain that the method of claim 49 would succeed, and that this success would be credible to one skilled in the art. Enablement of claim 49 does not require that the specification provide in vitro or in vivo experimental data.

Nevertheless, as further evidence that the claimed method would be expected to succeed, applicants attach hereto copies of Pagotto, et al. and Gillardon, et al. as **Exhibits 1 and 2** respectively, of the Supplemental Information Disclosure Statement.

Pagotto, et al. teach that the treatment of tumor cell lines with Zac1 antisense oligonucleotides (i.e. the molecule of claim 18) decreased the expression of the native Zac1 protein and caused increased cell proliferation. (See inter alia page 987, second column, second paragraph). Further, Pagotto, et al. teach that antisense oligonucleotides against Zac1 "controlled cell proliferation in a dose dependent way" (See abstract).

Gillardon, et al. describe delayed up-regulation of Zac1 in mice brains after transient local ischemia. Therefore, aggregation of Zac1 is shown to correlate with acute and/or chronic neuro-degenerative disorders, such as ischemia.

Applicants maintain that one of skill in the art would know how to make and use the claimed invention based on the specification, and would find the utility of the method of claim 49 credible. Therefore, the applicants submit that claim 49 satisfies the requirements of 35 U.S.C. §112, first paragraph.

The Examiner objected to claims 17-24, 36 and 39 as dependent on a rejected base claim. In response, applicants maintain that these claims, as well as new claim 49, are in condition for allowance for the reasons set forth above.

Applicants acknowledge the Examiner's statement that the instant claims are free of the prior art of record.

Supplemental Information Disclosure Statement

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents which are listed on Form PTO-1449 attached hereto as **Exhibit C** and also listed below.

Applicants submit this Supplemental Information Disclosure Statement after issuance of the first Office Action on the merits. Therefore, applicants enclose a check in the amount of $685.00, which amount includes the extension fee and the $240.00 fee pursuant to 37 CFR 1.17(p). Copies of the documents listed below as items 1 and 2 are attached hereto as **Exhibits 1 and 2.**

1. Pagotto, et al., (1999) "Inhibition of Zac1, a New Gene Differentially Expressed in the Anterior Pituitary, Increases Cell Proliferation", Endocrinology, 140, No.2, 987-996.

2. Gillardon, et al., (1998) "Delayed Up-regulation of Zac1 and PACAP Type I Receptor after Transient Focal Cerebral Ischemia in Mice", Molecular Brain Research, 61, 207-210.

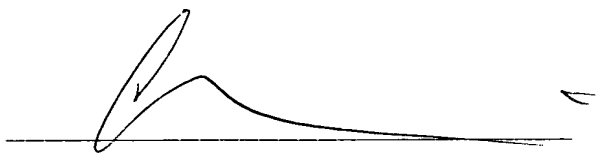
CONCLUSION

In view of the remarks and amendments made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejection. Applicants respectfully submit that the claims pending are in condition for allowance.

If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $445.00 for a three-month extension of time and $240.00 as set forth in 37 C.F.R. 1.17(p), is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Assistant Commissioner for Patents, Washington, D.C. 20231.

9/6/01
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Version with Markings to Show Changes Made

This application is ~~the~~ a national stage application filed ~~phase~~ under 35 U.S.C. §371 of ~~prior~~ PCT International Application No. PCT/EP97/05198, ~~which has an International filing date of~~ filed September 22, 1997, which designated the United States of America as a continuation-in-part of U.S. Serial No. 08/718,661, filed September 23, 1996, now U.S. Patent No. 5,876,972, issued March 2, 1999. The contents of these applications are incorporated herein by reference.

Version with Markings to Show Changes Made

17. (Amended) ~~The~~ A nucleic acid molecule ~~of claim 16~~ encoding a protein having the biological activity of a tumor suppressor, wherein the nucleic acid molecule comprises (a) a nucleotide sequence encoding the amino acid sequence given in SEQ ID NO.: 17 or (b) the nucleotide sequence given in SEQ ID NO.: 16.

18. (Twice Amended) A nucleic acid molecule of at least 15 nucleotides in length hybridizing specifically with (a) the nucleic acid molecule of claim 17, (b) a nucleic acid molecule comprising SEQ ID NO.: 1, (c) a nucleic acid molecule encoding the amino acid sequence of SEQ ID NO.: 2, or (d) a sequence complementary to that of (a), (b), or (c) ~~or to a complementary strand thereof~~.

19. (Twice amended) A vector comprising ~~a~~ the nucleic acid molecule of claim ~~1~~ 17.

20. (Amended) The vector of claim 19, wherein the nucleic acid molecule is operatively linked to regulatory elements permitting expression in prokaryotic ~~and/~~or eukaryotic host cells.

36. (Amended) A method for detecting expression of ~~the~~ a tumor suppressor in a cell by detecting the presence of mRNA coding for ~~a~~ the tumor suppressor which comprises:

(a) obtaining mRNA from ~~a~~ the cell;

(b) contacting the mRNA so obtained with a probe comprising a nucleic acid molecule of ~~claim 18~~ at least 15 nucleotides in length which, under stringent hybridizing conditions, hybridizes specifically to a nucleic acid molecule

(i) coding for the amino acid sequence of SEQ ID NO.: 2,
(ii) comprising the nucleotide sequence of SEQ ID NO.: 1,
(iii) coding for the amino acid sequence of SEQ ID NO.:17,
(iv) comprising the nucleotide sequence of SEQ ID NO.: 16, or
(v) having a sequence complementary to the nucleic acid molecule as defined in (i), (ii), (iii), or (iv) ~~under hybridizing conditions~~; and

(c) detecting the presence of mRNA specifically hybridized to the probe, ~~and~~ thereby detecting the expression of the tumor suppressor by the cell.

39. (Amended) A method for diagnosing in a subject a predisposition to a tumor or to a disorder associated with the expression of a tumor suppressor allele which comprises:

(a) isolating DNA from victims of the tumor or disorder;

(b) digesting t he isolated DNA of step (a) with at least one restriction enzyme;

(c) electrophoretically separating the resulting DNA fragments on a sizing gel;

(d) contacting the resulting gel with a probe labeled with a detectable marker comprising a nucleic acid molecule of ~~claim 18~~ at least 15 nucleotides in length which, under stringent hybridizing conditions, hybridizes specifically to a nucleic acid molecule

(i) coding for the amino acid sequence of SEQ ID NO.: 2,

(ii) comprising the nucleotide sequence of SEQ ID NO.:1,

(iii) coding for the amino acid sequence of SEQ ID NO.:17,

(iv) comprising the nucleotide sequence of SEQ ID NO.: 16, or

(v) having a sequence complementary to the nucleic acid molecule as defined in (i),(ii),(iii), or (iv)

~~labeled with a detectable marker~~;

(e) detecting labeled bands on a gel which have been hybridized to the probe as defined in (d) to create a band pattern specific to the DNA of the victims of the tumor or the disorder;

(f) preparing subject's DNA by steps (a) to (e) to produce detectable labeled bands on a gel; and

(g) comparing the band pattern specific to the DNA of victims of the tumor or the disorder of step (e) and the subject's DNA of step (f) to determine whether the patterns are the same or different and to diagnose thereby predisposition to the tumor or the disorder if the patterns are the same.

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